ScienSage

Journal of Advanced Scientific Research

Available online through http://www.sciensage.info

ISSN
0976-9595
Research Article

SYNTHESIS AND ANTIBACTERIAL STUDIES OF NEW ANALOGS OF 2-PYRAZOLINE FROM HALOGEN SUBSTITUTED α, β UNSATURATED AROMATIC KETONE

G.B. Rahatikar[1], S.N. Lakhekar[2], M.A. Baseer*[3]

[1]*Kai. Babasaheb Deshmukh Gorthekar Mahavidyalaya, Umri, India*

[2]*Chintamani College of Arts and Science, Gondpipri, India*

[3]*P.G. Research Chemistry Laboratory, Yeshwant College, Nanded, India*

**Corresponding author: dr.baseer.nanded@gmail.com*

ABSTRACT

Pyrazoline are familiar and important nitrogen containing five member heterocyclic compounds. Halogenated pyrazoline are widely studied for their antimicrobial activities. Present projection associated with a novel series of substituted 2-pyrazoline were prepared by the reaction with halogen substituted α, β unsaturated aromatic ketone i.e chalcones and hydrazine hydrate using alkaline condition. The newly synthesized 2-pyrazolines were characterized according to their physical constant and spectroscopic data. All the novel synthesized compounds were tested by their antibacterial action in *vitro* disc diffusion method against two gram +ve and two gram -ve bacteria. Synthesized compounds shows moderate to good activity.

Keywords: Halogenated pyrazoline, Antibacterial activity, Alkaline condition.

1. INTRODUCTION

Halogens are an important building block in the chemical and pharmaceutical industry. Some halogenated pyrazolines comounds have been account for their noteworthy biological activities such as monoamine oxidase inhibitory activity [1], antiproliferative activity [2], anticancer [3], antifungal [4], antitubercular [5], antitumour [6], antibacterial [7], antioxidant [8], antiviral [9], anti-parasitic [10],insecticidal [11], anti-inflammatory [12], antidiabetic [13], antidiuretic [14], antianalgesic [15], antihelminthic [16], antihypolipaemic [17], antimalerial [18] etc. usually these compounds are synthesized by substituted chalcones and hydrazine hydrate via one step reaction by cyclization [19].

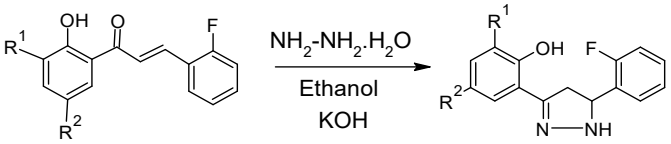
In these work, we account the synthesis of a novel derivative of halogenated pyrazoline through cyclization reaction. Halogenated chalcones and hydrazine hydrate by reflux on heating 50°C temperature give product. All the compounds formed in different time of reaction up to 3 to 4 hrs. Then all the molecules evaluated for their antibacterial activity.

2. EXPERIMENTAL

2.1. Synthesis of pyrazolines

The substitutes chalcones **[20]** were used for synthesis. The chemicals hydrazine hydrate (99.9%), ethanol and potassium hydroxide were obtained from SD Fine chemical limited and were used for carried out the reaction without purification. The solvent was purified as per the standard procedure. Reflux method is used for synthesis of pyrazolines **2(a-e)**.

All the newly prepared compounds were identified by spectral data (IR, ^{1}H-NMR, and Mass) which is reliable with the projected structures.



1(a-e) 2(a-e)

Table1. Substitution pattern and yield for compound 2(a-e)

Product	R_1	R_2	M.P. (°C)	Experi-mental Yield %	Colour
2a	I	Cl	170	73	Pale yellow
2b	Br	Cl	180	72	Yellow
2c	I	I	182	58	Yellow
2d	Br	Br	185	60	Dark yellow
2e	Br	CH_3	182	70	Black

2.2. Chemistry

The Melting points of synthesized compounds were determined in open capillary tube using melting point equipment and are uncorrected. IR spectra recorded with Shimadzu FT-IR machine by KBr pellets. ^{1}H-NMR spectra recorded in deuterated ($CDCl_3$) at an EA 400MHZ using NMR spectrophotometer. Reaction was checked by thin Layer chromatography (TLC) using silica gel plate pet ether, ethyl acetate (7:3 v/v) as a eluent system. The spot on silica gel plate were visualized in an ultraviolet cabinet at λ= 254-266nm.

2.3. General Procedure for Synthesis of Pyrazolines

Mixture of suitable chalcone (0.001mol) dissolved in 15 ml of ethanol solvent and hydrazine hydrate (0.002mol). To make the mixture basic a KOH (0.001mol) was added. Then the given mixture refluxed for 3-4hrs the progress of the reaction was time to time monitored by TLC using pet ether, ethyl acetate (7:3 v/v) as a eluent. After completion of reaction, the reaction mixture was cooled to room temperature and transferred in ice cold water (100 ml). Filter the given refluxed mixture to separate the solid product, washed and after drying recrystalized from ethanol.

2.3.1. 2a. 4-chloro-2-[5-(2-fluorophenyl)-4,5-dihydro-1H-pyrazol-3-yl]-6-iodophenol

IR(KBr, cm^{-1}): 3402 (Ar-OH), 3296 (N-H), 1595 (C=N); ^{1}H-NMR($CDCl_3$): δ 12.9(s, 1H, OH), 7.2-7.9 (m, 6H, Ar-H), δ 5.90 (s,1H, NH), δ 3.7 (dd, 1H, H_X), δ 3.0 (dd, 1H, H_A), δ 3.3 (dd, 1H, H_B), Mass: (M^+): *m/z* 416.

2.3.2. 2c. 6-[5-(2-fluorophenyl)-4,5-dihydro-1H-pyrazol-3-yl]-2,4-diiodocyclohexa-1,3-dien-1-ol

IR (KBr, cm^{-1}): 3400 (Ar-OH), 3202 (N-H), 1580 (C=N); ^{1}H-NMR($CDCl_3$): δ 13.12(s, 1H, OH), 7.5-7.8(m, 6H, Ar-H), δ 5.92 (s,1H, NH), δ 4.3 (dd, 1H, H_X), δ 3.2 (dd, 1H, H_A), δ 3.5 (dd, 1H, H_B), Mass: (M^+): *m/z* 510.

2.3.3. 2b. 2-bromo-4-chloro-6-[5-(2-fluorophenyl)-4,5-dihydro-1H-pyrazol-3-yl]cyclohexa-1,3-dien-1-ol

IR (KBr, cm^{-1}): 3410 (Ar-OH), 3200 (N-H), 1570 (C=N); ^{1}H-NMR($CDCl_3$): δ 13.9(s, 1H, OH) 12.8(s, 1H, OH), δ 7.5-8.0 (m, 5H , Ar-H), δ 5.96 (s,1H, NH), 2.25(s,3H, CH_3), δ 4.5 (dd, 1H, H_X), δ 3.8 (dd, 1H, H_B), δ 3.2 (dd, 1H, H_A), Mass: (M^+): *m/z* 371.

3. RESULTS AND DISCUSSION

3.1. Antimicrobial activity

The Disc-diffusion examine (Kirby-Bauer method) was used for the probable work. *In vitro* antimicrobial exploit was screened by means of Mueller Hinton Agar (MHA) obtained from Himedia (Mumbai). The MHA plate was arranged by pouring 15 ml of molten media into disinfected Petri plates. The plates were allowed to coagulate for 5 min and 0.1 % inoculums deferment was swabbed consistently and the Inoculums allowed to dry for 5 min. The concentration of compounds were set at (10 µg/disc) were weighed down on 5 mm sterile personage discs. The encumbered discs were placed on the exterior of medium and the compound was permissible to diffuse for 5 min and the plates were set aside for incubation at 37°C for 24 h. Penicillin (10 µg/disc) was used as positive control. At the end of incubation, inhibition zones formed in the region of the disc were measured with noticeable ruler in millimeter. (**Table 2**)

Table 2: Antimicrobial Activity

Sample	Zone of inhibition (mm)			
	Gram +ve Bacteria		Gram -ve Bacteria	
	B. subtilis	*S. aureus*	*E.coli*	*S. typhi*
Penicillin	28mm	26mm	30 mm	28 mm
2a	18	17	15	16
2b	11	13	08	09
2c	21	19	18	20
2d	10	12	09	07
2e	18	19	15	17

4. CONCLUSION

We have reported some new halogenated pyrazoline derivatives using substituted chalcones using hydrazine hydrate with good yield. These pyrazoline compounds were analysed by their physical constant and spectroscopic data. *In-vitro* antimicrobial behaviour was studied by disc diffusion method using two gram +ve and -ve bacteria. Some of the compounds showed moderate activity. However compound 2c show good activity against all four pathogen. It contain three halogen F, Cl, Br. Compound 2a and 2e also contain halogen and show moderate activity as compare to standard. Compound 2b contain two I as bulky halogen show less activity as compare to other compound.

Compound 2d having CH_3 group which shows less activity. It can be concluded that the -I effect of halogen always enhance the activity as compared with the standard.

5. ACKNOWLEDGEMENT

Authors would like to acknowledge PG Research Chemistry center, Yeshwant College, Nanded Maharashtra, India for providing all the chemicals and facilities for research work. Authors would like to express gratitude to the Principal of College their Constant support.

6. REFERENCES

1. Koç GS, Tan OU, Uçar G, Yıldırım E, Erol K, Palaska E. *Drug Res*, 2014; **64:**591-598.
2. Rao BS, Akberali PM, Holla BS, Sarojini BK. *J. Pharmacol. Toxicol*, 2008; **3:**102-110
3. Yang W, Hu Y, Yang YS, Zhang F, Zhang YB, Wang XL, et al. *Bioorg. Med. Chem,*2013; **21:**1050-1063.
4. Sharshira EM, Hamada NM. *Molecules*, 2012; 1**7:**4962-4971.
5. Horrocks P, Pickard MR, Parekh HH, Patel SP, Pathak RB. *Org. Biomol. Chem,* 2013; **11**:4891-4898.
6. Taylor EC, Patel HH. *Tetrahedron*, 1992; **48:**8089-8100.
7. Rashad AE, Shamroukh AH, Hegab MI, Awad HM. *Acta Chim. Slov*, 2005; **52:**429-434.
8. Baseer MA, Rahatikar GB, Patel AS, Vidule RR. *Int.J.Uni.Sci.Tech*, 2018; **3:**169-173.
9. Rashad AE, Hegab MI, Abdel-Megeid RE, Micky JA. *Bioorg. Med. Chem*, 2008; **16:** 7102-7106.
10. Bhat BA, Dhar KL, Saxena AK, Shanmugavel M, Qazi GN. *Bioorg. Med. Chem. Lett*, 2005; **15:**3177-3180
11. Kalirajan R, Sivakumar SU, Jubie S, Gowramma B, Suresh B. *Int. J. ChemTech Res*, 2009; **1:**27-34.
12. Holla BS, Akberali PM, Shivanada MK. *Farmaco*, 2000; **55:** 256-263.
13. Maggio B, Daidone G, Raffa D, Plescia S, Mantione L, Cutuli VM. *Eur. J. Med. Chem*, 2001; **36:**737-742.
14. Patil SY, Oswal RJ, Sayare AS, Landge SL, Antre RV, *Der Pharma Chemica.*, 2012; **1:**33-38.
15. Sawant AB, Gill CH, Nirwan RS. *Ind J Het Chem*, 2012; **21:**297-300.
16. Kotla VV, Dalavai VK, Chundari VR. *Der Pharma Chemica*, 2012; **4:**2003-2008.
17. Patel MR, Dodiya BL, Chetiya RM, Joshi KA, Vekaria PB, Bapodara AH et al. *Int. J. ChemTech Res*, 2011; **3:**967-974.
18. Acharya BN, Saraswat D, Tiwari M, Shrivastva AK, Ghorpade R, Bapna S et al. *Eur. J. Med. Chem*, 2010; **45:**430-438.
19. Yusuf M, Jain P. *Arab. J. Chem*, 2014; **7:**553-596.
20. Baseer MA, Rahatikar GB. *OAIJSE, 2018*; **3:**7-9.